

## REMARKS

### **I. Claims 1 & 2 Meet The 35 USC § 112 Written Description Requirement**

The Examiner asserts written description is lacking by explaining that:

Apart from disclosing that the entire SEQ ID NO:3 (AE') and at best the 102-nucleotide nucleic acid stem-loop forming sequence of SEQ ID NO:91 (AE'') within SEQ ID NO: 3 confer an age-associated stable gene expression pattern, the instant specification fails to describe any other essential core structural elements within the SEQ ID NO: 3 that have an age regulatory activity.

*Office Action p. 5.* The Applicants disagree because a sufficient number of age-regulatory sequences are taught to fulfill the *Lilly* "genus claim" standards. In this regard, it should be stressed that the specification provides actual sequences for portions of SEQ ID NO:3. This is in contrast to cases where the Federal Circuit has found written description lacking, i.e. cases where the sequence sought to be claimed was simply unknown and was claimed functionally (not structurally). The Examiner's citations to these cases is not appropriate. Indeed, the Examiner appears to overlook the fact that the specification 1) demonstrates that SEQ ID NO:3 has the specified activity (that is to say, there can be no question that it works in the manner taught), and 2) that portions of SEQ ID NO:3 also have the specified activity. With respect to the latter, the Examiner is asked to take note of Examples 11 and 12 wherein constructs containing AE'' are actually tested and found to work (Figure 17C).<sup>1</sup> Nonetheless, without waiving these arguments or acquiescing to the Examiner's rejection, but to further the prosecution, and hereby expressly reserving the right to prosecute the original (or similar) claims, Applicants have amended Claim 1 and Claim 2 to recite an age regulatory sequence consisting of a portion of SEQ ID NO:3 defined by SEQ ID NO:93 or a portion of SEQ ID NO:93 comprising SEQ ID NO:91.

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<sup>1</sup> The Examiner is requested to note that the *Office Action* pg 5 refers to AE'' as SEQ ID NO:91. That is not correct. SEQ ID NO:91 is properly identified as "a portion of" AE'' (i.e., SEQ ID NO:93) and "a portion of" AE' (i.e., SEQ ID NO:3). *Applicants' Specification* pg 39 ln 25-27.

## **II. Claims 1 & 2 Are Enabled**

The Examiner believes that the specification "... does not reasonably provide enablement for other recombinant expression vector[s] containing any other portions of SEQ ID NO:3 as an age-regulatory sequence or in any other operable combinations or a method of introducing a transgene into a cell *in vivo*. *Office Action* pg. 7. The Examiner improperly attempts to limit the Applicants' claims to SEQ ID NO:3 (i.e., AE3'; *Applicants' Specification* pg 30 *ln 11-12*) or SEQ ID NO:91 (a portion of AE3") *Applicants' Specification* pg 36 *ln 9-10*) by suggesting that only these specific sequences are enabled.

Again, the Examiner appears to overlook the fact that the specification contains data showing operability of SEQ ID NO:3 and portions thereof. Applicants submit a genus claim is particularly appropriate where what is being claimed is merely shorter lengths of the same sequence – in the face of working examples with such shorter species.

The Examiner's gene therapy arguments are without merit. The present claims are not directed to "cures." Patent law does not demand a demonstration of ultimate utility in order to satisfy enablement. The Examiner must take note of the fact that, as of the priority date (and even earlier), the FDA permitted many Phase I clinical trials to proceed, even though the techniques involved were not optimized. Enablement is shown in these reports by virtue of a) gene expression, and b) *some* therapeutic benefit.<sup>2</sup> That the "full promise" of gene therapy is not yet realized is irrelevant to patent law.

The Examiner's "gene therapy art was and still remains unpredictable" argument is – in the face of the many reports where both gene expression and therapeutic benefit are shown – simply misguided. That there will be gene expression *in vivo* is predictable. Only the *degree* of therapeutic benefit is difficult to predict. With respect to the present claims, no degree of therapeutic benefit is specified.

The Examiner appears to overlook the fact that the present invention offers an improvement in gene expression. Claim 1 specifies the standard components of an expression vector – together with sequences found by the present inventors to provide more predictable expression. And how were these age-related sequences proven to be of value? By *in vivo* expression studies in mice! The mere speculations of the Examiner are completely rebutted by these *in vivo* studies.

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<sup>2</sup> The Examiner can find these reports quite readily on PubMed. See for example, Human Gene Therapy 1998 Nov 20;9(17):2585-94 and Gene Therapy 1998 Nov;5(11):1538-44 and J. National Cancer Inst. 1999 May 5;91(9):763-71 – all of which describe successful expression *in vivo* and some anti-tumor success (albeit not complete).

It is particularly odd that the Examiner would cite references that indicate one of the main reasons that gene therapy has not achieved its full potential is “the lack of long term stable expression.” The age-related sequences of the present invention are the component that precisely address this issue!

The Examiner’s “underlying molecular mechanisms remain to be elucidated” argument has no place in patent law. It is not the duty of the applicants to provide “the underlying molecular mechanism” by which the age-related sequences achieve stable expression and/or enhanced expression over time. Patent law only demands that it work – not that applicants explain HOW it works.

Without waiving these arguments or acquiescing to the Examiner’s argument but to further the prosecution, and hereby expressly reserving the right to prosecute the original (or similar) claims, Applicants have amended Claim 1 and Claim 2 in the manner noted above. However, Claim 1 is by no means limited to only *in vitro* applications. To make this clear, Claim 13 has been amended to be dependent on Claim 1 and the Examiner is asked to permit Claim 14 to be included in the pending claims (since it is dependent on Claim 13). The Examiner is also requested that Claims 8 and 9 (amended now to be dependent on Claim 1) be included in the pending claims. Together, this would leave Claims 1-2, 8-9, 13-14 and 21 pending.

### **III. Claim 2 Is Not Indefinite**

The Examiner believes that “... due to the lack of a preamble and the opening language of the term “comprising”, it is unclear exactly which method that the Applicants intend to claim. The metes and bounds of the claim are not clearly determined”. *Office Action pg. 12*. The Applicants disagree. First, the Examiner is reminded that the “metes and bounds” of a patent claim is confined to the claim body, not the preamble. Second, there is no requirement for a patent claim to even have a descriptive preamble. Third, the Applicants’ choice of a transition term (i.e., comprising, consisting essentially of, or consisting of) is irrelevant to a proper interpretation of a preamble.

Nonetheless, without acquiescing to the Examiner’s argument but to further the prosecution, and hereby expressly reserving the right to prosecute the original (or similar) claims, Applicants have again amended Claim 2 to recite a method “of introducing a transgene into a cell”. This amendment is made not to acquiesce to the Examiner’s argument but only to further the Applicants’ business interests, better define one embodiment and expedite the prosecution of this application.

The Applicants respectfully request the Examiner withdraw the present indefiniteness rejection.

**IV. The Claims Are Not Anticipated**

As the Examiner is well aware, a single reference must disclose each limitation of a claim in order for that reference to anticipate the claim. *Atlas Powder Co. v. E.I. du Pont De Nemours & Co.*, 224 U.S.P.Q. 409, 411 (Fed. Cir. 1984). This criterion is not met with any of the cited references. The claims specify a particular portion of SEQ ID NO:3 - together with the term “consists of.” No reference teaches such a construct.

**V. Provisional Judicial Double Patenting Does Not Apply**

The Examiner believes that the claims recited in copending Application No. 11/129,861 are not patentably distinct for the presently claimed embodiment. The Applicants disagree. Moreover, the Examiner is asked to reconsider the rejection in view of the claim amendments described above.

**VI. A Priority Document Has Been Identified**

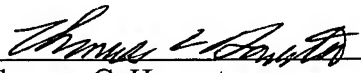
The Examiner apparently believes that a priority statement is not included within the specification. The Applicants disagree. A priority statement was properly made at the filing of the related PCT Application WO 00/75279 (filed: 6 June 2000) that identifies United States Patent Application 09/328,925 as a priority document. This filing is within sixteen months of the prior application, thereby no petition or fees are applicable.

The Examiner is referred to the “Amendments To The Specification” section for instructions as to the insertion of the appropriate priority statement.

**CONCLUSION**

The Applicants believe that the arguments and claim amendments set forth above traverse the Examiner's rejections and, therefore, request that all grounds for rejection be withdrawn for the reasons set above. Should the Examiner believe that a telephone interview would aid in the prosecution of this application, the Applicants encourage the Examiner to call the undersigned collect at 617.984.0616.

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